IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF WISCONSIN

NOVOZYMES A/S and NOVOZYMES NORTH AMERICA, INC.,	)	
Plaintiffs,	)	Case No. 10-CV-251
v.	)	PATENT CASE
DANISCO A/S, GENENCOR INTERNATIONAL WISCONSIN, INC., DANISCO US INC., and DANISCO USA INC.,	)	
Defendants.	)	

DANISCO'S MOTION FOR JUDGMENT AS A MATTER OF LAW THAT U.S. PATENT NO. 7,713,723 IS INVALID FOR LACK OF WRITTEN DESCRIPTION

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statutes

Other Authorities

Rules

Regulations

Pursuant to Rule 50(a) of the Federal Rules of Civil Procedure, Danisco moves for judgment as a matter of law that U.S. Patent No. 7,713,723 ("the '723 Patent") does not satisfy the written description requirement. To satisfy the written description requirement, the specification of U.S. Application No. 60/249,104 ("the 2000 Application") that Novozymes filed on November 16, 2000 must show that the named inventors *then possessed* the specific invention that Novozymes, with the benefit of a decade of hindsight, now claims in the '723 Patent. *See Ariad Pharms. v. Eli Lilly & Co.*, 598 F.3d 1336, 1355 (Fed. Cir. 2010) (en banc). As this Court put it, the inquiry is whether a person skilled in the art reading the specification in "2000 or 2001 [would have known] that making a substitution at position 239 would lead to increased thermostability under the claimed conditions." Opinion and Order dated Sept. 24, 2010 [Dkt. 106] ("PI Order") at 15.

The evidence admitted at trial falls far short of that standard. That evidence reveals a wide gulf between the very general specifications of the 2000 Application, which simply recited a laundry list of *many possible* types of alterations, *many possible* positions in the amino acid sequence to alter, *many possible* altered properties the resulting variant might exhibit, which together yield a *literally astronomical* number of possible variants, and the detailed and specific claims Novozymes filed 10 years later, after becoming aware of Danisco's innovative work in this area. Novozymes's hazy original 2000 Application does not even come close to pointing to a "substitution" (as opposed to a deletion or addition) at "position 239" (as opposed to one of 32 other positions, or a vast number of combinations of positions) in a BSG parent backbone (as opposed to any backbone with 60% homology to seven backbones listed in the

application), resulting in "increased thermostability" (as opposed to increases or decreases in an array of properties), at 90°C, 5 ppm calcium, and a pH of 4.5 (as opposed to a wide variety of other conditions). As Novozymes's *own expert* has conceded, persons skilled in the art looking at the 2000 Application would *not* conclude that the inventors possessed the particular *variant* Novozymes now claims, but rather were "in possession of a compelling and rational *design strategy* for the invention of alpha-amylases." 10/20/11 Tr. 4A at 65:19-22 (Davies) (emphasis added). There is no dispute of material fact that the disclosure of the 2000 Application is not legally sufficient to satisfy the written description requirement for the issued claims of the '723 Patent, and therefore the patent is invalid as a matter of law.

I. LEGAL STANDARD FOR JUDGMENT AS A MATTER OF LAW

Judgment as a matter of law is appropriate if "there is no legally sufficient evidentiary basis for a reasonable jury to find for [a] party on [an] issue . . . ." Fed. R. Civ. P. 50(a)(1). "In other words, the question is simply whether the evidence as a whole, when combined with all reasonable inferences permissibly drawn from that evidence, is sufficient to allow a reasonable jury to find in favor of the plaintiff." *Kahn v. Bland*, 630 F.3d 519, 523 (7th Cir. 2010) (quoting *Hall v. Forest River, Inc.*, 536 F.3d 615, 619 (7th Cir. 2008)).

II. NO REASONABLE JURY COULD CONCLUDE THAT THE EXTRAORDINARILY BROAD AND GENERAL DISCLOSURE OF THE 2000 APPLICATION PROVIDED ADEQUATE WRITTEN DESCRIPTION.

Federal law requires that a patent's "specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention." 35 U.S.C. § 112. "[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad*, 598 F.3d at 1351. "The question is not whether one skilled in this field of science might have been able to produce [the claimed invention] by building upon the teachings of the . . . Application, but rather whether that application 'convey[ed] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.'" *Goeddel v. Sugano*, 617 F.3d 1350, 1356 (Fed. Cir. 2010).

Claims added after the original disclosure are not part of the written description of the patent and cannot be considered as written description support for the claimed invention. *Anascape, Ltd. v. Nintendo of Am. Inc*., 601 F.3d 1333, 1337 (Fed. Cir. 2010); *see also Purdue Pharma, L.P. v. F.H. Faulding & Co.*, 48 F. Supp. 2d 420, 427 (D. Del. 1999) ("The policy behind the written description requirement is to prevent overreaching and post hoc claims that were not part of the original invention."), aff'd, 230 F.3d 1320 (Fed. Cir. 2000). As the Court has explained, the written description analysis cannot benefit from hindsight based on later-added claims; rather the proper inquiry is "whether the written description points the reader toward the claimed invention, not whether one can read the claims and work backward to search the specification for possible references to those claims." PI Order at 14.

The evidence at trial unequivocally indicates that a person skilled in the art, reading the original 2000 Application, would not conclude that in "2000 or 2001,"

Novozymes possessed "a substitution at position 239 [that] would lead to increased thermostability under the claimed conditions." PI Order at 15.

A. The Specification of the 2000 Application Literally Discloses More Variants than There Are Stars in the Sky.

As this Court has noted, the specification of the 2000 Application discloses an unusually high number of possible combinations. *See* Dkt. 185, Opinion and Order dated Feb. 4, 2011 ("SJ Order") at 11 (noting that "Plaintiffs do not contradict defendants' observation that, if plaintiffs' position is accepted, it means that plaintiffs disclosed 8.589 x 10^{42} possible inventions in their specifications."). The evidence adduced at trial makes clear that one skilled in the art would not be able to identify the specific variants claimed from among the enormous number set forth in the 2000 Application.

To begin with, the 2000 Application is not even directed to a single backbone, but potentially to countless backbones. Dkt. 726 at 42:16-19 (Raines) (testifying that "There's so many" potential backbones encompassed by the 2000 Application that "I can't even fathom."); *see also* Dkt. 713 at 40:10-11 (Andersen) ("there's a lot of [BLA] variants"); *id*. at 42:2-11 (Andersen) ("there is a number of alpha-amylases falling within [the specification]"). The specification states that *any* "other Termamyl-like alpha-amylases" can be used as the backbone so long as it "display[s] at least 60% . . . homology (identity) with at least one of said amino acid sequences shown in SEQ ID NOS: 2, 4, 6, 8, 10, 12, and 13." PX-1 at col.3, l.65-col.4, l.3. Therefore, the disclosure of the 2000 Application teaches that *any* of the numerous alpha-amylases that is at least 60% identical to any of the *seven* amino acid sequences listed may be used as the parent to create variants. Dkt. 726 at 42:20-23 (Raines) (testifying that the specification does not indicate whether any sequence is preferred over any others); *id*. at 43:5-11 (Raines)

("there's no direction to the reader to tell them to use a BSG alpha-amylase over any other alpha-amylase"). In addition, *hybrids* of one or more alpha-amylases qualify, so long as they satisfy the 60% requirement, DX-1012 at NZ0003912, making the number of potential backbones "mind-boggling." Dkt. 726 at 40:14-16. It is telling of the extreme breadth of that specification that the alpha-amylase actually used in practicing this invention is not the *Bacillus licheniformis* specifically mentioned in the specification, but *Bacillus stearothermophilus*.

The 2000 Application also lists 33 positions which can be altered. PX-1 at col.7, ll. 40-42. Dkt. 726 at 46:21-23 (Raines) (agreeing that under the 2000 Application alterations could be made at any of the 33 positions). "Not only does the specification identify 33 different positions, it identifies three different potential modifications (a substitution, a deletion or an insertion) . . . ." SJ Order at 9. *See generally* PX-1 at col.7, ll.45-51. One of skill in the art reading the 2000 Application would understand that it discloses *any combination* of insertions, deletions and substitutions at those 33 positions. Dkt. 713 at 54:19-20 (Andersen) ("because we invented each of the positions, so also the combination would be an invention"); Dkt. 726 at 46:10-20 (Raines). The 2000 Application discloses single, double, triple, and multiple substitutions. The specification identifies 41 "preferred embodiments" of single substitutions at the 33 positions. PX-1 at col.8, ll.10-14. It also identifies *250 preferred* "double, triple and multi-mutations" of substitutions at more than one of the 33 identified positions. PX-1 at col.8, l.25-col.16, l.20. Some of these preferred substitutions involve substitutions at as many as *15 positions*. PX-1 at col.16, ll.1-3.

Moreover, the 2000 Application also states that the variant can alter the stability of the enzyme to result in *either* "higher or lower stability," SJ Order at 9, at a variety of conditions. The 2000 Application states that the variant "exhibits an alteration in *at least* one of the following properties relative to said parent alpha-amylase: stability under, *e.g.*, high temperature and/or low pH conditions, in particular at low calcium concentrations." PX-1 at col.1, ll.30-33 (emphasis added). The specification states that "altered stability" is "improved stability (i.e., higher *or* lower)." PX-1 at col.16, ll.41-42 (emphasis added). Novozymes has argued that it would not make sense for enzymes used in industrial processes to have decreased stability at high termperatures, *see* SJ Order at 10, and the examples described in the specification involve variants with increased thermostability, *see* PX-1 at col.25, l.41; col.26, l.46. But the fact remains that Novozymes took pains in its specification to make clear that it was disclosing variants with *lower* stability; and indeed, one of the *preferred embodiments* recited in the specification—and the *only* one suggested for position 239, was a substitution of serine for the amino acid tryptophan (S239W), which even Novozymes admits does not increase thermostability. Dkt. 731 at 30:19-20 (Larsen); Dkt. 729 at 6:21-23 (Davies). It is evident that one of skill in the art reading the 2000 Application would understand that it discloses variants that both increase or decrease stability. Dkt. 726 at 50:17-51:2 (Raines) (if "you construct a molecule according to the disclosure . . . then you achieve altered stability" which is "defined in the 2000 application" to mean "higher stability or lower stability").

This Court noted the fact that the 2000 Application involved three types of variables as "the primary reason" it had concluded that there is a "substantial question about the written description" of the patent—the number of possible positions, the

different possible alterations (substitution, deletions, or insertion), and the different possible results (increased or decreased stability). SJ Order at 9. But in fact, the 2000 Application involves *still other* variables. Although the specific claim at issue here involves a variant that exhibits increased thermostability at a pH of 4.5, the specification discloses "mutations . . . of importance with respect to achieving altered stability, in particular improved stability (i.e., higher or lower), at . . . extreme pH (i.e., low or high pH, i.e., pH 4-6 or pH 8-11, respectively)." PX-1 at col.16, ll.39-47. One of skill in the art reading the 2000 Application would understand that it discloses altering stability at both at low pH values between 4 and 6, *and* high pH values between 8 and 11. Dkt. 713 at 65:5-11; 66:22-25; 69:8-14 (Andersen); Dkt. 726 at 52:8-17 (Raines). And although the specific claim here involves a temperature of 90°C, the 2000 Application discloses mutations that exhibit "improved stability (i.e., higher or lower), at especially high temperatures (i.e., 70-120° C) . . . ." PX-1 at col.16, ll.39-47. One of skill in the art reading the 2000 Application would understand that it discloses altering stability at *any* temperature within a range of 50 degrees Celsius (i.e., a range of 90 degrees Farenheit). Dkt. 713 at 63:21-24 (Andersen); Dkt. 726 at 51:16-19 (Raines). And although the specific claim at issue involves calcium concentrations of 5 ppm, the 2000 Application says that the invention relates to variants with increased thermostability "and/or at . . . low calcium concentration" which it defines as less than 60 ppm. PX-1 at col. 7, 11.18-21. One of skill in the art reading the 2000 Application would understand that it discloses altering stability at *any* calcium concentration level. Dkt. 726 at 52:1-7 (Raines) (Under the 2000 application, "you might be able to have an alpha-amylase

variant that has alpha-amylase activity at calcium concentrations of 5 ppm or 25 ppm or 40 ppm or lower than 60 ppm.").

The existence of such an incredibly high number of possible variants is fundamentally inconsistent with the suggestion that one skilled in the art looking at the 2000 Application would "immediately discern" the specific variant claimed here. *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000) ("one skilled in the art, reading the original disclosure, must immediately discern the limitation at issue in the claims"). A specification so broad constitutes insufficient written description as a matter of law, both because it plainly does not indicate possession of the specific variant at issue here, but also because "[a]n adequate written description . . . requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997). Such a patent is better described, as Novozymes's put it, as a "*design strategy* for the invention of alpha-amylases," 10/20/11 Tr. 4A at 65: 19-22 (Davies) (emphasis added), or, as the company's Regional President of North America explained, as setting forth "good spot[s] to pursue understanding." Dkt. 703 at 69:1-5 (Monroe); *see also id.* at 69:18-23 (Monroe) (testifying that "in 2005 is when we really started to understand that would be a good spot to do some work or that that could be of interest to make a better enzyme"). Under the law, however, an insight into what could be useful and patentable is not enough. "The patent laws do not reward an inventor's invitation to other researchers to discover which of the thousands of [possible variants] could conceivably work [for the claimed function]." *Boston Scientific Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1367 (Fed. Cir. 2011). "[A] patent is not a

hunting license. It is not a reward for the search, but compensation for its successful conclusion." *University of Rochester v. G. D. Searle & Co.*, 358 F.3d 916, 930 n.10 (Fed. Cir. 2004) (*quoting Brenner v. Manson*, 383 U.S. 519, 539 (1966)).

B. The 2000 Application Fails to Provide Any Blaze Marks Directing One of Skill in the Art to Narrow the Specification to Arrive at the Claimed Variants.

When a patent's specification identifies a large genus of compounds or recites options with a series of variables, the written description requirement is not met unless the specification discloses "blaze marks" that would lead one of skill in the art to understand that the patentee was in possession of the particular claimed invention when its patent application was filed. *See, e.g., Purdue Pharma*, 230 F.3d at 1326-27; *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570-71 (Fed. Cir. 1996) ("simply describing a large genus of compounds is not sufficient to satisfy the written description requirement as to particular species or sub-genuses"); *In re Ruschig*, 379 F.2d 990, 994-95 (C.C.P.A. 1967). "[I]n the absence of blaze marks 'as to what compounds other than those disclosed as preferred, might be of special interest . . . simply describing a large genus of compounds is not sufficient to satisfy the written description requirement as to particular species or sub-genuses.'" *Boston Scientific Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1367 (Fed. Cir. 2011) (*quoting Fujikawa*, 93 F.3d at 1570). The written description is not met when the claimed invention is included in a large genus of compounds and is not "specifically named or mentioned in any manner, [such that] one is left to selection from the myriads of possibilities encompassed by the broad disclosure, with no guide indicating or directing that this particular selection should be made rather than any of the many others which could also be made." *Application of Ruschig*, 379 F.2d 990, 995 (C.C.P.A. 1967) (quoting and affirming the Patent Office Board of Appeal's decision).

The evidence adduced at trial demonstrates that the disclosure of the 2000 Application falls woefully short of that minimum requirement. In order to arrive at the invention claimed in the '723 Patent, one of skill in the art would necessarily have to make numerous choices with respect to many variables. *Cf.* Dkt. 713 at 70:6-8 (Andersen) (agreeing that the specification is "broader" than the claim limitations); Dkt. 714 at 11:24-25 (Andersen) (admitting that the specification filed in 2000 is "very different from what was issued [in the claims of the '723 patent] in 2010"). In order to arrive at the claims as eventually issued, a person would need to

1. Choose from among the countless possible backbone options one that has at least 90% sequence identity to *Bacillus stearothermophilus*. Dkt. 726 at 42:16-19 (Raines) (answering he "can't even fathom" how many possible backbones are encompassed by the 2000 application).
2. Determine that of all possible combinations of insertions, deletions, and/or substitutions, that a substitution at only a single position should be made.
3. Determine that of the 33 positions listed in the 2000 Application, the substitution would be made only at position 239.
4. Determine that the relevant property to be altered would be thermostability.
5. Determine that altered thermostability would be increased rather than decreased.
6. Determine that from the pH ranges of 4-6 and 8-11, stability would be increased at pH 4.5.
7. Determine that from the temperature range of 70-120ºC, stability would be increased at 90°C.

8. Determine that from all possible calcium concentrations below 60 ppm, stability would be increased at 5 ppm.

9. Determine which of the 19 possible amino acids could be substituted at position 239 to achieve that result.

As set forth below, the disclosure in the 2000 Application provides "blaze marks" for *none* of those choices.

1. The 2000 Application Provides No Blaze Marks Directing One of Skill in the Art to the Claimed Backbone.

One of ordinary skill in the art reading the 2000 Application would find no direction to choose a backbone with at least 90% sequence identity to BSG over any of the countless other possible backbones disclosed. As Carsten Andersen conceded at trial, *all* possible backbones are "just as interesting" under the 2000 Application, Dkt. 713 at 43: 21-22 (Andersen), and BSG is not listed as a preferred embodiment. *Id.* 41:9-12 (Andersen); *see also* Dkt. 726 at 65:7-17 (Raines) ("There was no guidance to BSG in the 2000 application."). Nor do the Examples in the 2000 Application direct one of skill in the art to which of countless possible backbones to use, much less to the conclusion that the backbone should have at least 90% sequence identity to *Bacillus stearothermophilus*. Dkt. 726 at 65:7-66:6 (Raines). The Examples all use the *Bacillus licheniformis* backbone. PX-1 at col. 25, l.1-col.26, l.65. *None* of the variants in the Examples are variants of a *Bacillus stearothermophilus* alpha-amylase or have 90% or more sequence identity to SEQ ID NO: 6. PX-1 at col. 25, l.1-col.26, l.65; Dkt. 726 at 65:7-66:6 (Raines).

Indeed, the specification teaches away from using BSG. Mr. Andersen concedes that BSG is not among the several preferred embodiments listed. Dkt. 713 at 41:10-12.

In fact, one of skill in the art would read the Examples as teaching away from using a *Bacillus stearothermophilus* backbone or a backbone with at least 90% sequence identity to BSG. Dkt. 726 at 65:15-17 (Raines) ("The only enzymes that were – for which data were provided were the BLA variants."). Indeed, Mr. Andersen testified that he believed that the 2000 Application indicated that "BLA is the most important alpha-amylase." Dkt. 713 at 50:5. BSG is on the low end of the homology range established in the specification—about 65% homologous to BLA (Dkt. 713 at 30:17-19 (Andersen))—making it a *remote* possibility for a backbone when viewing from the legally-relevant perspective of 2000. Indeed, it is telling that BLA, which is the principal focus of the specification, *does not come within* the '723 Patent's claim's limitations of being 90% homologous to BSG. *Id.*

2. The 2000 Application Provides No Blaze Marks to Position 239.

One of ordinary skill in the art reading the 2000 Application would find no direction to choose an alteration at position 239 over any of the other 32 listed positions. Dkt. 713 at 45:20-21 (Andersen) (admitting that all 33 positions "are all equally important"); Dkt. 726 at 65:1-6 (Raines) ("The 33 positions were treated equally. There was no highlight in any way of position 239 in the 2000 application."). Even considering *only* substitutions (and not additions or deletions) on a *single backbone*, the list of 33 possible alteration sites in the 2000 Application yields a set of more than 8.589×10^{42} (i.e., 20^{33-1}) possible variants that may be made from *each* parent alpha-amylase. Dkt. 726 at 48:11-18 (Raines); *see also id.* at 48:21-49:3 (Raines) (To give you perspective on this number . . . "the number of stars that scientists believe exist in the universe is 10^{21}."). That literally astronomical number would climb even higher if it included variants

possible if insertions and deletions were also made, and higher still if consideration were given to the enormous number of alternative parent alpha-amylases in which the alterations can be made. Dkt. 726 at 48:11-18 (Raines) (noting that his calculation of 8.589×10^{42} is "only for making substitutions in one backbone, one parent" and "didn't include insertions or deletions").

However, the specification provides *no indication whatsoever* that variants with alterations at position 239 are the preferred method of locating that single star in the nighttime sky. Dkt. 726 at 49:4-8 (Raines) (the 2000 application provides "no guidance" to a person of ordinary skill in the art to make single substitutions or multiple substitutions). In fact, two of the '723 Patent's *named inventors* conceded that nothing in the 2000 Application pointed to position 239 over any of the other 32 listed positions. Dkt. 728-2 at 89:14-22 (Fuglsang) (conceding that he could not recall "anything in the '723 patent that points to position 239 in particular as important for thermal stability relative to any of the other [32] positions"); Dkt. 728-2, at 186:17-24 (Thisted) ("an alteration at 239 wouldn't be my first priority after reading the '723 patent"). The specification provides no clue that variants at position 239 warrant particular attention if one seeks to improve thermostability. Dkt. 726 at 65:23-66:6 (Raines) (answering that no disclosure nor any example of "any variant of BSG that would have increased thermostability" could be found in the 2000 Application, under any conditions, much less those claimed.).

The only data presented in the specification regarding any alterations resulting in "increased thermostability" and "alpha-amylase activity" are found in the Examples section. The Examples disclose 15 variants that reportedly increased stability at pH 4.5,

90 °C, and 5 ppm calcium. PX-1 at col.25, l.1-col.26, l.65; Dkt. 726 at 47:6-14 (Raines). But tellingly, the Examples section presents *no* data relating to position 239. PX-1 at col.25, l.1-col.26, l.65; Dkt. 726 at 47:2-5 (Raines). If the Examples are to be read, as Dr. Arnold and Dr. Davies argue, as directing one of skill in the art to the claimed invention, then one of skill in the art would understand, based on the Examples, that the specification is directed to variants with substitutions at positions *other than* position 239 (or any of the other 17 positions listed by Mr. Andersen). Dkt. 726 at 65:1-6 (Raines) (agreeing there is no instruction in the 2000 application to make variants at position 239 as opposed to any of the other positions). Since the majority of the variants for which data are present in the Examples section contain multiple substitutions and none contains a substitution at position 239, the Examples would point one of skill in the art, seeking to increase the stability of an alpha-amylase, *away from* making a single substitution in which serine is replaced at position 239. Dkt. 726 at 65:18-22 (Raines) (agreeing that there is "no example in the specification of a single BSG variant at any of the 33 positions, much less 239, that would actually have alpha-amylase activity.").

Nor does the specification state that any particular alterations will result in "increased thermostability" and "alpha-amylase activity" at pH 4.5, 90 ºC, and 5 ppm calcium. Rather, the specification only states that desirable properties "may result" from the "variants of the invention." PX-1 at col. 7, ll.4-5. Furthermore, the *only* substitution at position 239 listed in the specification is a tryptophan ("S239W") substitution. However, testing results show that this particular substitution results in *decreased* thermostability. *See* Dkt. 726 at 59:4-6 (Raines) ("We know that the S239 W variant does not have enhanced thermostability."). Therefore, the specification does not describe

any of the possible variants with alterations at position 239 that have the required "increased thermostability" and "alpha-amylase activity" for a variant within the claims. Dkt. 726 at 64:22-25 (Raines) (agreeing that the 2000 application does not describe any variant at position 230 that will have higher or lower thermostability at the particular claim conditions.").

3. The 2000 Application Provides No Blaze Marks Directing to the Claimed Type of Alteration.

One of ordinary skill in the art reading the 2000 Application would find no direction to choose substitutions as opposed to insertions or deletions. Dkt. 726 at 45:15-22 (Raines) ("[The 2000 application] says you can make any on of these. You can make an insertion, a deletion, or a substitution."). Although Novozymes's experts testified that one of skill in the art would choose substitutions because that is the type of alteration seen in the Examples section, as discussed above, the Examples do not use a backbone with at least 90% sequence identity to the *Bacillus stearothermophilus* backbone and the Examples do not include any alterations at position 239. *See* PX-1 at col.25, l.1-col.26, l.65; Dkt. 726 at 65:18-22 (Raines) (confirming there is "no example in the specification of a single BSG variant at any one of the 33 positions, much less 239"). Furthermore, claims 7, 9 and 12-15 of the '723 Patent are directed to insertions, deletions, or substitutions at one or more of 32 of the 33 positions in addition to a substitution at position 239. Dkt. 726 at 45:23-46:6 (Raines) ("the patent as a whole includes all three of these types of changes.").

In addition, the 2000 Application does not direct the reader to single alterations; it lists approximately 250 double, triple, and multiple alterations. *See* 10/20/11 Tr. 4A 9:18-21 (Davies) (testifying that specification does not say "how to choose among single,

double, triple, . . . multiple mutations" or indicate that one type is more important than others); Dkt. 726 at 49:4-8 (Raines) (stating there's "no guidance" on making single substitutions or multiple substitutions").

4. The 2000 Application Provides No Blaze Marks Directing to the Claimed Increased Thermostability Under Particular Conditions.

One of ordinary skill in the art reading the 2000 Application would find no direction to choose variants that result in increased thermostability at pH 4.5, 90°C and 5 ppm calcium. Dkt. 726 at 38:22-39:3 (Raines) (confirming he could not find any particular alterations that corresponded to an increased thermostability in the disclosure of the 2000 patent application). The specification discloses multiple beneficial properties including tolerance to low or high pH, as well as increased or decreased thermostability. Dkt. 726 at 50:20-51:7 (Raines). Furthermore, as discussed above, even if increased thermostability is chosen, one of skill in the art would need to know the claimed conditions under which such thermostability testing should be run. As discussed above, the 2000 Application provides ranges of possible pH values, temperature values, and calcium concentrations under which the testing could be done. PX-1 at col.16, ll.39-47; *see also* Dkt. 726 at 51:12-52:17 (Raines). Although the 2000 Application sets forth examples involving low pH, high temperature, and low calcium, as discussed above, the examples do not use a backbone with at least 90% sequence identity to the *Bacillus stearothermophilus* backbone and do not include any alterations at position 239. *See* PX-1 at col.25, l.1-col.26, l.65; Dkt. 726 at 65:18-22 (Raines). As such, one of skill in the art would find no blaze marks when reading the 2000 Application offering direction to variants with increased thermostability at pH 4.5, 90°C and 5 ppm calcium.

C. The 2000 Application's Mere *Ipsis Verbis* Disclosure of Only the Broad Genus in the Specification, Without Identifying Any Specific Species, Does Not Satisfy the Written Description Requirement.

It is not enough that the specification contains a perfunctory *ipsis verbis* disclosure of the broad genus that includes the specific variant claimed. *Boston Scientific Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1364 (Fed. Cir. 2011) ("An *ipsis verbis* disclosure of a claimed genus . . . is not *per se* sufficient to meet the written description requirement") (*citing Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 968 (Fed. Cir. 2002)); *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010) (en banc) ("[G]eneric claim language appearing *in ipsis verbis* in the original specification does not satisfy the written description requirement if it fails to support the scope of the genus claimed." (*citing Enzo Biochem*, 323 F.3d at 968)). Even if a "compound was within the literal scope of the originally filed claim, [it fails to meet the written description requirement if] it was never 'named or otherwise exemplified' in the appellants' original patent application." *University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 922 (Fed. Cir. 2004) (citing and explaining the holding of *In re Rushing*, 379 F.2d 990 (C.C.P.A. 1967)).

"To satisfy the written description requirement in the case of a chemical or biotechnological genus, more than a statement of the genus is normally required." *Carnegie Mellon Univ. v. Hoffman-La Roche Inc.*, 541 F.3d 1115, 1126 (Fed. Cir. 2008). As the Federal Circuit has explained, "'an adequate written description of a claimed genus requires more than a generic statement of an invention's boundaries.' . . . [A] patent must set forth 'either a representative number of species falling within the scope of the genus or structural features common to the members of the genus.'" *Billups-Rothenberg, Inc. v. Associated Regional and University Pathologists, Inc.*, 642 F.3d

1031, 1037 (Fed. Cir. 2011) (en banc) (internal citations omitted) (affirming summary judgment of invalidity for lack of written description where specification failed to disclose a single species satisfying the claims or structural characteristics of those that would); *see also* U.S. Patent & Trademark Ofc., *Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement*, 66 Fed. Reg. 1099, 1106 (2001) ("The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species."). That requirement is necessary so that "one of skill in the art can 'visualize or recognize' the members of the genus," *Boston Scientific Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1363 (Fed. Cir. 2011) (en banc) (quoting *Ariad Pharm., Inc. v. Eli Lilly & Co*., 598 F.3d 1336, 1350 (Fed. Cir. 2010), and must be sufficiently "precise" to allow that person to distinguish them from non-functional members of the genus. *Id.* (the written description of a genus must be "sufficient to distinguish it from other materials").

In a series of recent cases, the Federal Circuit has emphasized the centrality of this requirement, holding patents invalid for insufficient written description and ordering judgment as a matter of law where the patentee's generic description of the genus did not identify a particular species claimed. In *Boston Scientific*, for example, the court affirmed the grant of judgment as a matter of law in favor of a party challenging two parents, concluding that "no reasonable jury could conclude that there is sufficient written description for the asserted claims" 647 F.3d at 1363, where the specification for the patents identified only the genus of a drug (and certain analogs) to be used in stents. The court emphasized that a large number of possible analogs came within the specification's literal description, and noted that there was "no guidance at all in the

specification as to how to properly identify or choose the claimed analogs," *id.* at 1365, other than that they "must be 'structural[ly] similar' to [the drug] rapamycin." *Id.* at 1364. And in *Billup-Rothenberg v. Associated Regional & University Pathologists*, 642 F.3d 1031 (Fed. Cir. 2011), the Federal Circuit likewise ordered judgment as a matter of law for a defendant, finding insufficient written description where a patent claim for a genus where the specification failed to "set forth 'either a representative number of species falling within the scope of the genus or structural features common to the members of the genus.'" *Id.* at 1037 (quoting *Ariad*, 598 F.3d at 1349). *Accord Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1350 (Fed. Cir. 2011) (reversing denial of judgment as a matter of law for insufficient written description, because "while the patent broadly claims a class of antibodies that contain human variable regions, the specification does not describe a single antibody that satisfies the claim limitations"); *see also Carnegie Mellon*, 541 F.3d at 1125-26 (holding written description insufficient to support claimed genus where specifications only disclosed single species).

That line of cases plainly supports judgment as a matter of law here. As discussed above, the claims of the '723 Patent claim a functionally defined genus of isolated alpha-amylase variants with substitutions at position 239 in the *Bacillus stearothermophilus* alpha-amylase backbone: those with increased thermostability at the specific condition pH 4.5, 90° C and 5 ppm calcium. However, the 2000 Application does not identify even a single variant that falls within the scope of the claims. Dkt. 713 at 50:22-51:1 (Andersen) (admitting that "there is no disclosure in the 2000 application of any variant of at any enzyme that's 60% homologous to a BLA enzyme where it's modified at

position 239 [that increases thermostability]"); Dkt. 726 at 65:18-66:2 (Raines) (agreeing that there is no disclosure nor any example in the 2000 application of any BSG variant that would have increased thermostability). The only alteration at position 239 specifically listed in the 2000 Application is the S239W substitution, which "we know . . . does not have enhanced thermostability." Dkt. 726 at 59:4-6 (Raines). Furthermore, the specification presents no data demonstrating that Novozymes conducted any testing of *any* alteration at position 239, including the S239W substitution. PX-1; Dkt. 726 at 65:18-22 (Raines); Dkt. 713 at 31:5-21 (Andersen) (admitting the specification does not include testing data of any variant that meets the claim limitations); Dkt. 728-4 at 37:5-8 (Thisted) (admitting that "[t]here is no specific data relating to thermostability for [position 239]"). One of the other inventors conceded that he could not point to any language in the specification that would cause the reader to understand that a mutation at 239 would result in increased thermostability. Dkt. 728-3 at 77:2-12 (Kjaerulff) (conceding that he could not locate language in the specification "[w]here [] it say[s] that an alteration at position 239 will result in increased thermal stability"); *cf.* Dkt. 728-2 at 91:18-25 (Fuglsang) (testifying that he could not "point to any language in the '723 patent that would direct the reader to understand that a mutation at 239 would result in increased stability at low pH versus high pH").

D. There Was No Well-Known Correlation Between Structure and Function of the Claimed Alpha-Amylase Variants with Increased Thermostability.

The claims of the '723 Patent disclose a functionally defined genus of isolated alpha-amylase variants with substitutions at position 239 in the *Bacillus stearothermophilus* backbone: those with increased thermostability at pH 4.5, 90° C and

5 ppm calcium. To be sure, "[f]unctional claim language can meet the written description requirement." *Billups-Rothenberg*, 642 F.3d at 1037 (quoting *Ariad*, 598 F.3d at 1349). However, functional language is only adequate to satisfy that requirement when "the art has established a correlation between structure and function." *Id.* Any such correlation between alpha-amylase structure and the claimed function of increased thermostability was neither known in the art in 2000-2001 or disclosed in the 2000 Application. Dkt. 713 at 37:6-9 (Andersen) (admitting "there's no connection [in the specification] between the function at low calcium concentrations and the structure of the calcium binding site in the 2000 disclosure").

There was no well-known relationship between structure and the claimed function that would allow a person of skill in the art to distinguish without experimentation which variants that would have increased thermostability and which will not. Dkt. 726 at 58:1-7 (Raines). One study by a group that included a Nobel Laureate published in 2000 identified 15 sites on *Bacillus licheniformis* that researchers believed, based on the crystal structure of the alpha-amylase, "could be important determinants of protein stability." DX-1033. But after extensive testing, they found that some of the variants at only 3 of the 15 positions resulted in creased thermostability; most or all of the variants at 5 of the 15 positions were generally neutral; and most or all of the variants at 7 of the 15 positions were *detrimental* to thermostability. *Id.* In 2003, the same published another paper addressing the stability of the *Bacillus licheniformis* alpha-amylase, in which they observed that "examples of engineered mutations resulting in effects opposite to the ones expected are legion. . . . Elucidating the origin of thermal stability for a given protein and finding ways to increase it remains a specific and challenging task." DX-1150. The

answers of even Novozymes's witnesses who profess to greater confidence in structure-function relationships reveal the limitations on understanding even now. *See* Dkt. 729 at 8:13-17 (Davies) (conceding he could not tell from studying the "crystal structure" of an alpha-amylase which substitution at position 239 would enhance thermostability); Dkt. 713 at 55 (Andersen) (stating that he did not know whether any of the approximately 250 preferred embodiments worked); *see also* Dkt. 728-2, at 84:17-22 (Fuglsang) (testifying that it "would be a speculation and guessing before you have conducted all studies" to predict whether "every position in this list [of 33 positions in the 2000 Application], if altered from the wild type, would provide a variant with increased thermal stability at low pH, high temperature, [and] low calcium").

Neither the prior art nor the 2000 Application itself provide sufficient description to distinguish between those species falling within the claimed functional genus from those that do not. Consequently, the disclosure in the 2000 Application falls short of that required to describe the functionally claimed genus of substitutions at position 239 resulting in increased thermostability. *See Ariad*, 598 F.3d at 1350 ("[A] sufficient description of a genus instead requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members so that one of skill in the art can 'visualize or recognize' the members of the genus."). Under the proper analysis, the 2000 Application does not adequately describe the claimed invention: the specification neither identifies alpha-amylase variants falling within the scope of the claims nor provides any blaze marks to those that do. It does not matter how mature or sophisticated Novozymes attempts to argue the art was; the fact is Novozymes can point to no evidence, either in the prior art or in the 2000 Application, to

show a known structure-function relationship for the claimed increased thermostability functional limitation.

Moreover, the evidence introduced at trial of the extensive testing Danisco performed to prepare the variant at position 239 that was the subject of its '026 Patent confirms the inadequacy of the written description. If one skilled in the art would have known from the 2000 Application alone that a substitution at position 239 would yield increased thermostability, the millions of dollars Danisco spent in testing would have been utterly unnecessary to enable it to develop that variant. The fact that Danisco went to such lengths is a compelling confirmation that the written description in the applications leading to the '723 Patent was entirely inadequate.

E. The Specification's Lists of Positions and Substitutions Are Not Each Alternatively Usable For the Purposes of the Invention.

During the parties' summary judgment briefing on written description, Novozymes relied on *Application of Driscoll*, 562 F.2d 1245 (CCPA 1977), to argue that the 2000 Application need not include any blaze marks to position 239. Novozymes asserted that because position 239 appeared in a *Markush* group with 32 other positions in the 2000 Application, those of skill in the art would understand that alterations at *each* of the 33 positions would lead to increased thermostability. Dkt. 149, Novozymes's Opposition to Danisco's Motion for Summary Judgment at 46-48. But even Novozymes's expert witness does not consider all 33 to be alternatively usable, but rather acknowledges that one must "make and test" them to know whether they will work. Dkt. 729 at 8:9-12 (Davies). And even the inventors of the '723 Patent testified that they do not know whether each of the 33 listed positions will result in a variant with increased thermostability. Dkt. 328-3 at 78:1-9 (Kjaerulff) (conceding that he does not know if

"every substitution that can be made at each of the 33 positions . . . of the '723 patent will result in an alpha-amylase variant with [] increased thermal stability"); Dkt. 328-4 at 54:9-13 (Thisted) (admitting that he does not know if "alterations at any of these 33 positions will result in increased thermostability"); Dkt. 328-2 at 84:17-22 (Fuglsang) (stating that it "would be [] speculation and guessing" to say that every position on the list in the 2000 Application "would provide a variant with increased thermal stability at low pH, high temperature, low calcium").

Consequently, contrary to Novozymes's assertion, those of skill in the art do not view the list of *all* 33 positions as "alternatively usable" for increasing thermostability and *Driscoll* does not excuse the 2000 Application's failure to include blaze marks in position 239. *See* Dkt. 185, Motion for Summary Judgment Order at 8 (explaining that *Markush* groups can be used to describe multiple possibilities "so long as each is 'alternatively usable for the purposes of the invention'"). *See generally Driscoll*, 562 F.2d at 1249-50 (description adequate so long as "one skilled in the art would view" the description as providing for use of any one of fourteen alternative compounds).

F. The Testimony of Frances Arnold, Ph.D. Was Based on a Legally Erroneous Standard and Is Entitled to No Weight as a Matter of Law.

The testimony of plaintiffs' expert, Dr. Frances Arnold, was made under an improper standard and thus is entitled to no weight as a matter of law. As the Court has explained, the proper inquiry is "whether the written description points the reader toward the claimed invention, not whether one can read the claims and work backward to search the specification for possible references to those claims." Opinion and Order dated Sept. 24, 2010, [Dkt. No. 106] at 14 ("PI Order"). But despite that explicit guidance, Dr. Arnold improperly worked backward, starting with Novozymes's 2009 claims and

looking backward to cherry pick from portions of the specification that support the claims. Dr. Arnold had no choice but to work backward because there are no blaze marks in the '723 patent specification that point to position 239, so she instead uses Novozymes's later-filed claim as a substitute. Her flawed testimony is entitled to no weight. *Cf.* Fed. R. Evid. 702.

The claims of the '723 patent cannot be considered to support the description of the claimed invention. Claims added after the original disclosure are not part of the written description and cannot be considered as written description support for the claimed invention. *Anascape, Ltd. v. Nintendo of Am. Inc.*, 601 F.3d 1333, 1337 (Fed. Cir. 2010); *see also Purdue Pharma, L.P. v. F.H. Faulding & Co.*, 48 F. Supp. 2d 420, 427 (D. Del. 1999), aff'd, 230 F.3d 1320 (Fed. Cir. 2000) ("The policy behind the written description requirement is to prevent overreaching and post hoc claims that were not part of the original invention."). The specificity provided by those later-added claims cannot be considered in determining whether there is written description for the claimed invention. Nor can the claims of the '723 Patent be used to guide the written description analysis today. When the specification identifies a large genus of compounds or recites options at a series of variables, the specification must contain "blaze marks" to reasonably lead those skilled in the art to the claimed species or sub-genuses. *Boston Scientific*, 647 F.3d at 1367; *In re Ruschig*, 379 F.2d 990, 994-95 (CCPA 1967).

Dr. Arnold's written description analysis directly conflicts with the analysis set out by both the Federal Circuit and this Court. Despite the Court's specific instruction that it was impermissible to "work backward" from the claims, Dr. Arnold did just that to reach her opinion that the asserted claims are not invalid for lack of written description.

Indeed, her testimony suggested that considering the 33 positions without the guidance of the later-filed claims yielded an impossibly large number of combinations. Although the specification does not specifically point to position 239 as opposed to any of the other 32 positions and does not identify which substitutions at position 239 will result in a variant with increased thermostability, she used those portions of the claims to serve as "blaze marks" to guide her analysis. Written description is to be determined by reviewing the specifications from the perspective of one skilled in the art "as of the filing date." *Ariad*, 598 F.3d at 1351. Because her testimony concerned an improper inquiry, it is entitled to no weight.

III. CONCLUSION

There is no legally sufficient evidentiary basis for a reasonable jury to find for Novozymes on the issue of written description, and therefore, judgment as a matter of law for Danisco is appropriate. As discussed above, the 2000 Application discloses an enormous number of disclosed variants. To sort through all of these disclosed variants to arrive at the invention eventually claimed in the '723 Patent, one skilled in the art would need to narrow the specification in a very particular manner. The 2000 Application, however, provides no blaze marks directing one of skill in the art to narrow the specification in this manner. Specifically, the specification fails to provide any blaze marks directing one of skill in the art to the claimed backbone, the claimed position 239, the claimed alteration (i.e., a substitution), and to the claimed increased thermostability under very particular conditions, individually or in combination. Moreover, neither the prior knowledge of one of skill in the art nor the specification itself establishes a structure-function relationship for the claimed increased thermostability. The specification also fails to identify a single variant that satisfies the claim limitations.

Furthermore, Novozymes's *Markush* argument fails since both parties' experts as well as Novozymes's named inventors admit that the list of 33 positions are *not* alternatively usable for creating a variant with increased thermostability. Similarly, the 19 possible substitutions at each of the 33 positions are also not alternatively usable for creating a variant with increased thermostability. Accordingly, the 2000 Application fails to provide adequate written description to the eventually-issued claims of the '723 Patent and the patent is invalid.

Dated: October 21, 2011

Respectfully submitted,

/s/ Tracey B. Davies

Tracey B. Davies
Michael A. Valek
Stephen C. Stout
VINSON & ELKINS LLP
The Terrace
2801 Via Fortuna, Suite 100
Austin, TX 78746-7568
Tel: 512-542-8400
Fax: 512-542-8612
tdavies@velaw.com
mvalek@velaw.com
sstout@velaw.com

John P. Elwood
VINSON & ELKINS LLP
2200 Pennsylvania Ave., NW
Suite 500W
Washington, DC 20037
Tel: 202-639-6500
Fax: 202-639-6604
jelwood@velaw.com

Of Counsel:

Kendall Harrison
Todd G. Smith
GODFREY & KAHN
One East Main Street
Madison, WI 53703
Tel: 608-257-3911
Fax: 608-257-0609
kharrison@gklaw.com
tsmith@gklaw.com

William Dawson
GIBSON DUNN
2100 McKinney Avenue, Suite 1100
Dallas, Texas 75201
Tel: 214-698-3132
Fax: 214-571-2919
wdawson@gibsondunn.com

Attorneys for Defendants Danisco A/S, Genencor International Wisconsin, Inc., Danisco US Inc., and Danisco USA Inc.

US 1097875v.1